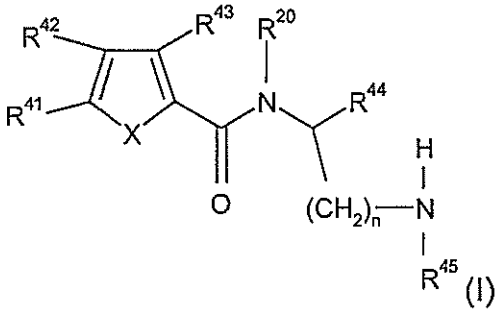
Claims

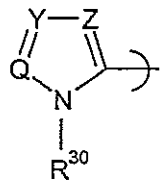
1. A compound of Formula (I),



(I)

wherein:

R^{41} is selected from: chlorine, ethyl, methyl and methoxy;

R^{42} is ,

where Q is nitrogen, Y is –CH- and Z is –C(R^{48})-, and R^{30} is selected from methyl and ethyl, where R^{48} is selected from: hydrogen, methyl, chlorine and bromine;

R^{43} is hydrogen;

R^{44} is –CH_2-phenyl wherein the phenyl is substituted by one or two substituents selected from fluorine and trifluoromethyl;

R^{45} is hydrogen;

R^{20} is hydrogen;

X is selected from O and S; and

n is 1;

or a pharmaceutically acceptable salt thereof.

2. A compound of claim 1 selected from:

N-((1S)-2-amino-1-{[2-(trifluoromethyl)phenyl]methyl}ethyl)-5-chloro-4-(1-methyl-1H-pyrazol-5-yl)-2-thiophenecarboxamide;
N-((1S)-2-amino-1-{[2-(trifluoromethyl)phenyl]methyl}ethyl)-4-(4-bromo-1-methyl-1H-pyrazol-5-yl)-5-methyl-2-thiophenecarboxamide;
N-((1S)-2-amino-1-{[2-(trifluoromethyl)phenyl]methyl}ethyl)-4-(4-chloro-1-methyl-1H-pyrazol-5-yl)-5-methyl-2-thiophenecarboxamide;
N-((1S)-2-amino-1-{[2-(trifluoromethyl)phenyl]methyl}ethyl)-5-chloro-4-(4-chloro-1-methyl-1H-pyrazol-5-yl)-2-thiophenecarboxamide;
N-((1S)-2-amino-1-{[2-(trifluoromethyl)phenyl]methyl}ethyl)-4-(4-bromo-1-methyl-1H-pyrazol-5-yl)-5-chloro-2-thiophenecarboxamide;
N-((1*S*)-2-amino-1-{[2-(trifluoromethyl)phenyl]methyl}ethyl)-5-methyl-4-(1-methyl-1*H*-pyrazol-5-yl)-2-thiophenecarboxamide;
N-((1*S*)-2-amino-1-{[2-(trifluoromethyl)phenyl]methyl}ethyl)-5-chloro-4-(1-ethyl-1*H*-pyrazol-5-yl)-2-thiophenecarboxamide;
N-((1*S*)-2-amino-1-{[2-(trifluoromethyl)phenyl]methyl}ethyl)-5-chloro-4-(1,4-dimethyl-1*H*-pyrazol-5-yl)-2-thiophenecarboxamide;
-4-(1-methyl-1*H*-pyrazol-5-yl)-2-thiophenecarboxamide;
N-{(1*S*)-2-amino-1-[(3-fluorophenyl)methyl]ethyl}-5-chloro-4-(4-chloro-1-methyl-1*H*-pyrazol-5-yl)-2-thiophenecarboxamide;
N-((1S)-2-amino-1-{[2-(trifluoromethyl)phenyl]methyl}ethyl)-5-ethyl-4-(1-methyl-1H-pyrazol-5-yl)-2-thiophenecarboxamide;
N-((1S)-2-amino-1-{[2-(trifluoromethyl)phenyl]methyl}ethyl)-4-(1,4-dimethyl-1H-pyrazol-5-yl)-5-methyl-2-thiophenecarboxamide;
N-((1S)-2-amino-1-{[2-(trifluoromethyl)phenyl]methyl}ethyl)-4-(4-chloro-1-methyl-1H-pyrazol-5-yl)-5-ethyl-2-thiophenecarboxamide;
N-((1S)-2-amino-1-{[2-(trifluoromethyl)phenyl]methyl}ethyl)-4-(4-bromo-1-methyl-1H-pyrazol-5-yl)-5-ethyl-2-thiophenecarboxamide;
N-((1S)-2-amino-1-{[2-(trifluoromethyl)phenyl]methyl}ethyl)-4-(1,4-dimethyl-1H-pyrazol-5-yl)-5-ethyl-2-thiophenecarboxamide;
N-((1S)-2-amino-1-{[2-(trifluoromethyl)phenyl]methyl}ethyl)-5-methyl-4-(1-methyl-1H-pyrazol-5-yl)-2-furancarboxamide;
N-((1S)-2-amino-1-{[2-(trifluoromethyl)phenyl]methyl}ethyl)-4-(4-bromo-1-methyl-1H-pyrazol-5-yl)-5-methyl-2-furancarboxamide;
N-((1S)-2-amino-1-{[2-(trifluoromethyl)phenyl]methyl}ethyl)-4-(4-chloro-1-methyl-1H-pyrazol-5-yl)-5-methyl-2-furancarboxamide;
N-((1S)-2-amino-1-{[2-(trifluoromethyl)phenyl]methyl}ethyl)-4-(1,4-dimethyl-1H-pyrazol-5-yl)-5-methyl-2-furancarboxamide;

N-{(1S)-2-amino-1-[(3-fluorophenyl)methyl]ethyl}-4-(4-chloro-1-methyl-1H-pyrazol-5-yl)-5-ethyl-2-thiophenecarboxamide;
N-{(1S)-2-amino-1-[(3-fluorophenyl)methyl]ethyl}-4-(1,4-dimethyl-1H-pyrazol-5-yl)-5-ethyl-2-thiophenecarboxamide;
N-((1S)-2-amino-1-{[3-(trifluoromethyl)phenyl]methyl}ethyl)-4-(1,4-dimethyl-1H-pyrazol-5-yl)-5-ethyl-2-thiophenecarboxamide;
N-((1S)-2-amino-1-{[2-(trifluoromethyl)phenyl]methyl}ethyl)-5-chloro-4-(1-methyl-1H-pyrazol-5-yl)-2-furancarboxamide;
N-((1S)-2-amino-1-{[2-(trifluoromethyl)phenyl]methyl}ethyl)-5-chloro-4-(4-chloro-1-methyl-1H-pyrazol-5-yl)-2-furancarboxamide;
N-((1S)-2-amino-1-{[2-(trifluoromethyl)phenyl]methyl}ethyl)-4-(4-chloro-1-methyl-1H-pyrazol-5-yl)-5-ethyl-2-furancarboxamide;
N-{(1S)-2-amino-1-[(4-fluorophenyl)methyl]ethyl}-4-(4-chloro-1-methyl-1H-pyrazol-5-yl)-5-ethyl-2-furancarboxamide;
N-{(1S)-2-amino-1-[(3-fluorophenyl)methyl]ethyl}-4-(4-chloro-1-methyl-1H-pyrazol-5-yl)-5-ethyl-2-furancarboxamide;
N-{(1S)-2-amino-1-[(3-fluorophenyl)methyl]ethyl}-5-chloro-4-(1-methyl-1H-pyrazol-5-yl)-2-furancarboxamide;
N-{(1S)-2-amino-1-[(4-fluorophenyl)methyl]ethyl}-5-chloro-4-(1-methyl-1H-pyrazol-5-yl)-2-furancarboxamide;
N-((1S)-2-amino-1-{[3-(trifluoromethyl)phenyl]methyl}ethyl)-5-chloro-4-(1-methyl-1H-pyrazol-5-yl)-2-furancarboxamide;
N-{(1S)-2-amino-1-[(3-fluorophenyl)methyl]ethyl}-5-chloro-4-(4-chloro-1-methyl-1H-pyrazol-5-yl)-2-furancarboxamide;
N-((1S)-2-amino-1-{[3-(trifluoromethyl)phenyl]methyl}ethyl)-5-chloro-4-(4-chloro-1-methyl-1H-pyrazol-5-yl)-2-furancarboxamide;
N-{(1S)-2-amino-1-[(4-fluorophenyl)methyl]ethyl}-5-chloro-4-(4-chloro-1-methyl-1H-pyrazol-5-yl)-2-furancarboxamide;
N-{(1S)-2-amino-1-[(3-fluorophenyl)methyl]ethyl}-5-chloro-4-(1,4-dimethyl-1H-pyrazol-5-yl)-2-furancarboxamide;
N-{(1S)-2-amino-1-[(4-fluorophenyl)methyl]ethyl}-5-chloro-4-(1,4-dimethyl-1H-pyrazol-5-yl)-2-furancarboxamide;
N-((1S)-2-amino-1-{[3-(trifluoromethyl)phenyl]methyl}ethyl)-5-chloro-4-(1,4-dimethyl-1H-pyrazol-5-yl)-2-furancarboxamide;
N-((1S)-2-amino-1-{[2-(trifluoromethyl)phenyl]methyl}ethyl)-5-chloro-4-(1,4-dimethyl-1H-pyrazol-5-yl)-2-furancarboxamide;

N-((1*S*)-2-amino-1-{[3-(trifluoromethyl)phenyl]methyl}ethyl)-5-methyl-4-(1-methyl-1*H*-pyrazol-5-yl)-2-thiophenecarboxamide;
N-{(1*S*)-2-amino-1-[(4-fluorophenyl)methyl]ethyl}-5-chloro-4-(1-methyl-1*H*-pyrazol-5-yl)-2-thiophenecarboxamide;
N-((1*S*)-2-amino-1-{[3-(trifluoromethyl)phenyl]methyl}ethyl)-5-chloro-4-(1-methyl-1*H*-pyrazol-5-yl)-2-thiophenecarboxamide;
N-{(1*S*)-2-amino-1-[(4-fluorophenyl)methyl]ethyl}-5-methyl-4-(1-methyl-1*H*-pyrazol-5-yl)-2-thiophenecarboxamide;
N-{(1*S*)-2-amino-1-[(3-fluorophenyl)methyl]ethyl}-5-methyl-4-(1-methyl-1*H*-pyrazol-5-yl)-2-thiophenecarboxamide;
N-((1*S*)-2-amino-1-{[3-(trifluoromethyl)phenyl]methyl}ethyl)-4-(4-chloro-1-methyl-1*H*-pyrazol-5-yl)-5-methyl-2-thiophenecarboxamide;
N-{(1*S*)-2-amino-1-[(4-fluorophenyl)methyl]ethyl}-4-(4-bromo-1-methyl-1*H*-pyrazol-5-yl)-5-methyl-2-thiophenecarboxamide;
N-{(1*S*)-2-amino-1-[(4-fluorophenyl)methyl]ethyl}-4-(4-chloro-1-methyl-1*H*-pyrazol-5-yl)-5-methyl-2-thiophenecarboxamide;
N-{(1*S*)-2-amino-1-[(3-fluorophenyl)methyl]ethyl}-4-(4-chloro-1-methyl-1*H*-pyrazol-5-yl)-5-methyl-2-thiophenecarboxamide;
N-{(1*S*)-2-amino-1-[(3-fluorophenyl)methyl]ethyl}-4-(4-bromo-1-methyl-1*H*-pyrazol-5-yl)-5-methyl-2-thiophenecarboxamide;
N-((1*S*)-2-amino-1-{[3-(trifluoromethyl)phenyl]methyl}ethyl)-4-(4-bromo-1-methyl-1*H*-pyrazol-5-yl)-5-methyl-2-thiophenecarboxamide;
N-((1*S*)-2-amino-1-{[3-(trifluoromethyl)phenyl]methyl}ethyl)-4-(1,4-dimethyl-1*H*-pyrazol-5-yl)-5-methyl-2-thiophenecarboxamide;
N-{(1*S*)-2-amino-1-[(3-fluorophenyl)methyl]ethyl}-4-(1,4-dimethyl-1*H*-pyrazol-5-yl)-5-methyl-2-thiophenecarboxamide;
N-{(1*S*)-2-amino-1-[(4-fluorophenyl)methyl]ethyl}-4-(1,4-dimethyl-1*H*-pyrazol-5-yl)-5-methyl-2-thiophenecarboxamide;
N-{(1*S*)-2-amino-1-[(3-fluorophenyl)methyl]ethyl}-4-(4-bromo-1-methyl-1*H*-pyrazol-5-yl)-5-chloro-2-thiophenecarboxamide;
N-((1*S*)-2-amino-1-{[3-(trifluoromethyl)phenyl]methyl}ethyl)-5-chloro-4-(4-chloro-1-methyl-1*H*-pyrazol-5-yl)-2-thiophenecarboxamide;
N-((1*S*)-2-amino-1-{[3-(trifluoromethyl)phenyl]methyl}ethyl)-4-(4-bromo-1-methyl-1*H*-pyrazol-5-yl)-5-chloro-2-thiophenecarboxamide;
N-{(1*S*)-2-amino-1-[(4-fluorophenyl)methyl]ethyl}-4-(4-bromo-1-methyl-1*H*-pyrazol-5-yl)-5-chloro-2-thiophenecarboxamide;

N-{(1*S*)-2-amino-1-[(4-fluorophenyl)methyl]ethyl}-5-chloro-4-(4-chloro-1-methyl-1*H*-pyrazol-5-yl)-2-thiophenecarboxamide;
N-{(1*S*)-2-amino-1-[(2,5-difluorophenyl)methyl]ethyl}-4-(4-chloro-1-methyl-1*H*-pyrazol-5-yl)-5-methyl-2-thiophenecarboxamide;
N-{(1*S*)-2-amino-1-[(2,5-difluorophenyl)methyl]ethyl}-5-methyl-4-(1-methyl-1*H*-pyrazol-5-yl)-2-thiophenecarboxamide;
N-{(1*S*)-2-amino-1-[(2,5-difluorophenyl)methyl]ethyl}-4-(1,4-dimethyl-1*H*-pyrazol-5-yl)-5-methyl-2-thiophenecarboxamide;
N-{(1*S*)-2-amino-1-[(2,5-difluorophenyl)methyl]ethyl}-5-chloro-4-(4-chloro-1-methyl-1*H*-pyrazol-5-yl)-2-thiophenecarboxamide;
N-{(1*S*)-2-amino-1-[(2,5-difluorophenyl)methyl]ethyl}-5-chloro-4-(1-methyl-1*H*-pyrazol-5-yl)-2-thiophenecarboxamide;
N-{(1*S*)-2-amino-1-[(3-fluorophenyl)methyl]ethyl}-4-(4-chloro-1-methyl-1*H*-pyrazol-5-yl)-5-methyl-2-furancarboxamide;
N-((1*S*)-2-amino-1-{[2-(trifluoromethyl)phenyl]methyl}ethyl)-5-(methyloxy)-4-(1-methyl-1*H*-pyrazol-5-yl)-2-thiophenecarboxamide;
N-{(1*S*)-2-amino-1-[(4-fluorophenyl)methyl]ethyl}-4-(4-chloro-1-methyl-1*H*-pyrazol-5-yl)-5-methyl-2-furancarboxamide;
N-((1*S*)-2-amino-1-{[3-(trifluoromethyl)phenyl]methyl}ethyl)-4-(4-chloro-1-methyl-1*H*-pyrazol-5-yl)-5-methyl-2-furancarboxamide;
N-((1*S*)-2-amino-1-{[2-(trifluoromethyl)phenyl]methyl}ethyl)-4-(4-chloro-1-methyl-1*H*-pyrazol-5-yl)-5-(methyloxy)-2-thiophenecarboxamide;
N-{(1*S*)-2-amino-1-[(2,5-difluorophenyl)methyl]ethyl}-5-chloro-4-(1,4-dimethyl-1*H*-pyrazol-5-yl)-2-thiophenecarboxamide;
N-{(1*S*)-2-amino-1-[(3-fluorophenyl)methyl]ethyl}-4-(4-chloro-1-methyl-1*H*-pyrazol-5-yl)-5-(methyloxy)-2-thiophenecarboxamide;
N-{(1*S*)-2-amino-1-[(4-fluorophenyl)methyl]ethyl}-4-(4-chloro-1-methyl-1*H*-pyrazol-5-yl)-5-(methyloxy)-2-thiophenecarboxamide;
N-((1*S*)-2-amino-1-{[3-(trifluoromethyl)phenyl]methyl}ethyl)-4-(4-chloro-1-methyl-1*H*-pyrazol-5-yl)-5-(methyloxy)-2-thiophenecarboxamide;
N-{(1*S*)-2-amino-1-[(4-fluorophenyl)methyl]ethyl}-4-(1,4-dimethyl-1*H*-pyrazol-5-yl)-5-ethyl-2-thiophenecarboxamide;
N-{(1*S*)-2-amino-1-[(3,4-difluorophenyl)methyl]ethyl}-5-methyl-4-(1-methyl-1*H*-pyrazol-5-yl)-2-thiophenecarboxamide;
N-{(1*S*)-2-amino-1-[(3,4-difluorophenyl)methyl]ethyl}-4-(4-chloro-1-methyl-1*H*-pyrazol-5-yl)-5-methyl-2-thiophenecarboxamide;

N-{(1*S*)-2-amino-1-[(3,4-difluorophenyl)methyl]ethyl}-5-chloro-4-(1-methyl-1*H*-pyrazol-5-yl)-2-thiophenecarboxamide;
N-{(1*S*)-2-amino-1-[(3,4-difluorophenyl)methyl]ethyl}-5-chloro-4-(4-chloro-1-methyl-1*H*-pyrazol-5-yl)-2-thiophenecarboxamide;
N-{(1*S*)-2-amino-1-[(3,4-difluorophenyl)methyl]ethyl}-4-(1,4-dimethyl-1*H*-pyrazol-5-yl)-5-methyl-2-thiophenecarboxamide;
N-{(1*S*)-2-amino-1-[(3,4-difluorophenyl)methyl]ethyl}-5-chloro-4-(4-chloro-1-methyl-1*H*-pyrazol-5-yl)-2-furancarboxamide;
N-{(1*S*)-2-amino-1-[(3,4-difluorophenyl)methyl]ethyl}-5-chloro-4-(1-methyl-1*H*-pyrazol-5-yl)-2-furancarboxamide;
N-{(1*S*)-2-amino-1-[(3,4-difluorophenyl)methyl]ethyl}-5-methyl-4-(1-methyl-1*H*-pyrazol-5-yl)-2-furancarboxamide;
N-{(1*S*)-2-amino-1-[(3,4-difluorophenyl)methyl]ethyl}-4-(4-chloro-1-methyl-1*H*-pyrazol-5-yl)-5-methyl-2-furancarboxamide;
N-{(1*S*)-2-amino-1-[(3,4-difluorophenyl)methyl]ethyl}-5-chloro-4-(1,4-dimethyl-1*H*-pyrazol-5-yl)-2-furancarboxamide;
N-{(1*S*)-2-amino-1-[(3,4-difluorophenyl)methyl]ethyl}-4-(1,4-dimethyl-1*H*-pyrazol-5-yl)-5-methyl-2-furancarboxamide;
N-((1*S*)-2-amino-1-{[2-(trifluoromethyl)phenyl]methyl}ethyl)-5-chloro-4-(4-chloro-1-ethyl-1*H*-pyrazol-5-yl)-2-thiophenecarboxamide;
N-{(1*S*)-2-amino-1-[(3-fluorophenyl)methyl]ethyl}-5-chloro-4-(4-chloro-1-ethyl-1*H*-pyrazol-5-yl)-2-thiophenecarboxamide;
N-{(1*S*)-2-amino-1-[(4-fluorophenyl)methyl]ethyl}-5-chloro-4-(4-chloro-1-ethyl-1*H*-pyrazol-5-yl)-2-thiophenecarboxamide;
N-((1*S*)-2-amino-1-{[3-(trifluoromethyl)phenyl]methyl}ethyl)-5-chloro-4-(4-chloro-1-ethyl-1*H*-pyrazol-5-yl)-2-thiophenecarboxamide;
N-((1*S*)-2-amino-1-{[2-(trifluoromethyl)phenyl]methyl}ethyl)-5-chloro-4-(1-ethyl-4-methyl-1*H*-pyrazol-5-yl)-2-thiophenecarboxamide;
N-{(1*S*)-2-amino-1-[(3-fluorophenyl)methyl]ethyl}-5-chloro-4-(1-ethyl-4-methyl-1*H*-pyrazol-5-yl)-2-thiophenecarboxamide;
N-{(1*S*)-2-amino-1-[(3,4-difluorophenyl)methyl]ethyl}-5-chloro-4-(1-ethyl-4-methyl-1*H*-pyrazol-5-yl)-2-thiophenecarboxamide;
N-{(1*S*)-2-amino-1-[(3-fluorophenyl)methyl]ethyl}-5-chloro-4-(1,4-dimethyl-1*H*-pyrazol-5-yl)-2-thiophenecarboxamide;
N-((1*S*)-2-amino-1-{[3-(trifluoromethyl)phenyl]methyl}ethyl)-5-chloro-4-(1,4-dimethyl-1*H*-pyrazol-5-yl)-2-thiophenecarboxamide;

N-{(1*S*)-2-amino-1-[(4-fluorophenyl)methyl]ethyl}-5-chloro-4-(1,4-dimethyl-1*H*-pyrazol-5-yl)-2-thiophenecarboxamide;
N-{(1*S*)-2-amino-1-[(3,4-difluorophenyl)methyl]ethyl}-5-chloro-4-(4-chloro-1-ethyl-1*H*-pyrazol-5-yl)-2-thiophenecarboxamide;
N-{(1*S*)-2-amino-1-[(3,4-difluorophenyl)methyl]ethyl}-5-chloro-4-(4-chloro-1-ethyl-1*H*-pyrazol-5-yl)-2-furancarboxamide; and
N-{(1*S*)-2-amino-1-[(3,4-difluorophenyl)methyl]ethyl}-4-(4-chloro-1-ethyl-1*H*-pyrazol-5-yl)-5-methyl-2-furancarboxamide;

or a pharmaceutically acceptable salt thereof.

3. A compound of claim 1 selected from:
N-{(1*S*)-2-amino-1-[(3-fluorophenyl)methyl]ethyl}-5-chloro-4-(4-chloro-1-methyl-1*H*-pyrazol-5-yl)-2-thiophenecarboxamide;
N-{(1S)-2-amino-1-[(3-fluorophenyl)methyl]ethyl}-5-chloro-4-(4-chloro-1-methyl-1H-pyrazol-5-yl)-2-furancarboxamide;
N-{(1*S*)-2-amino-1-[(3-fluorophenyl)methyl]ethyl}-4-(4-chloro-1-methyl-1*H*-pyrazol-5-yl)-5-methyl-2-thiophenecarboxamide;
N-{(1*S*)-2-amino-1-[(3,4-difluorophenyl)methyl]ethyl}-5-chloro-4-(4-chloro-1-methyl-1*H*-pyrazol-5-yl)-2-thiophenecarboxamide;
N-{(1*S*)-2-amino-1-[(3,4-difluorophenyl)methyl]ethyl}-5-chloro-4-(4-chloro-1-methyl-1*H*-pyrazol-5-yl)-2-furancarboxamide;
or a pharmaceutically acceptable salt thereof.

4. A compound of claim 1 which is:
N-{(1*S*)-2-amino-1-[(3-fluorophenyl)methyl]ethyl}-5-chloro-4-(4-chloro-1-methyl-1*H*-pyrazol-5-yl)-2-thiophenecarboxamide;
or a pharmaceutically acceptable salt thereof.

5. A compound of claim 1 which is:
N-{(1*S*)-2-amino-1-[(3,4-difluorophenyl)methyl]ethyl}-5-chloro-4-(4-chloro-1-methyl-1*H*-pyrazol-5-yl)-2-furancarboxamide;
or a pharmaceutically acceptable salt thereof.

6. A compound according to any one of claims 1 to 5, or a pharmaceutically acceptable salt thereof, for use in therapy.

7. Use of a compound defined in any one of claims 1 to 5 or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating or lessening the severity of a disease or condition selected from cancer and arthritis.

8. The use according to claim 7 wherein said cancer is selected from: brain (gliomas), glioblastomas, Bannayan-Zonana syndrome, Cowden disease, Lhermitte-Duclos disease, breast, inflammatory breast cancer, Wilm's tumor, Ewing's sarcoma, Rhabdomyosarcoma, ependymoma, medulloblastoma, colon, head and neck, kidney, lung, liver, melanoma, ovarian, pancreatic, prostate, sarcoma, osteosarcoma, giant cell tumor of bone, thyroid, Lymphoblastic T cell leukemia, Chronic myelogenous leukemia, Chronic lymphocytic leukemia, Hairy-cell leukemia, acute lymphoblastic leukemia, acute myelogenous leukemia, Chronic neutrophilic leukemia, Acute lymphoblastic T cell leukemia, Plasmacytoma, Immunoblastic large cell leukemia, Mantle cell leukemia, Multiple myeloma Megakaryoblastic leukemia, multiple myeloma, acute megakaryocytic leukemia, promyelocytic leukemia, Erythroleukemia, malignant lymphoma, hodgkins lymphoma, non-hodgkins lymphoma, lymphoblastic T cell lymphoma, Burkitt's lymphoma, follicular lymphoma, neuroblastoma, bladder cancer, urothelial cancer, lung cancer, vulval cancer, cervical cancer, endometrial cancer, renal cancer, mesothelioma, esophageal cancer, salivary gland cancer, hepatocellular cancer, gastric cancer, nasopharangeal cancer, buccal cancer, cancer of the mouth, GIST (gastrointestinal stromal tumor) and testicular cancer.

9. The use according to claim 8 wherein said cancer is selected from: brain (gliomas), glioblastomas, Bannayan-Zonana syndrome, Cowden disease, Lhermitte-Duclos disease, breast, colon, head and neck, kidney, lung, liver, melanoma, ovarian, pancreatic, prostate, sarcoma and thyroid.

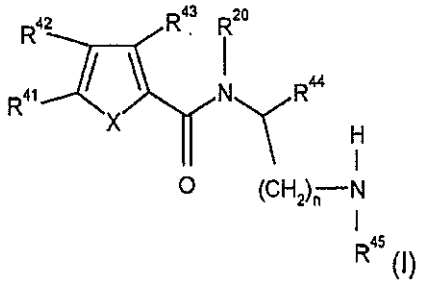
10. A pharmaceutical composition comprising a compound according to any one of claims 1 to 5, or a pharmaceutically acceptable salt thereof and a pharmaceutically acceptable carrier.

11. The pharmaceutical composition according to claim 10 which further comprises at least one anti-neoplastic agent.

12. The pharmaceutical composition according to claim 11 wherein the at least one anti-neoplastic agent is selected from the group consisting essentially of anti-microtubule agents, platinum coordination complexes, alkylating agents, antibiotic agents, topoisomerase II inhibitors, antimetabolites, topoisomerase I inhibitors, hormones and hormonal analogues, signal transduction pathway inhibitors; non-receptor tyrosine kinase angiogenesis inhibitors; immunotherapeutic agents; proapoptotic agents; and cell cycle signaling inhibitors.

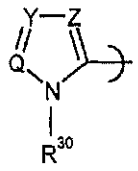
Claims

1. A compound of Formula (I),



wherein:

R^{41} is selected from: chlorine, ethyl, methyl and methoxy;
$R4^2$ is



where Q is nitrogen, Y is -CH- and Z is -C(R^{48})-, and R^{30} is selected from methyl and ethyl, where R^{48} is selected from: hydrogen, methyl, chlorine and bromine;
R^{43} is hydrogen;
R^{44} is -CH_2-phenyl wherein the phenyl is substituted by one or two substituents selected from fluorine and trifluoromethyl;
R^{45} is hydrogen;
R^{20} is hydrogen;
X is selected from O and S; and
n is 1;
or a pharmaceutically acceptable salt thereof.

2. A compound of claim 1 selected from:

N-((1S)-2-amino-1-{[2-(trifluoromethyl)phenyl]methyl}ethyl)-5-chloro-4-(1-methyl-1 H-pyrazol-5-yl)-2-thiophenecarboxamide;
N-((1S)-2-amino-1-{[2-(trifluoromethyl)phenyl]methyl}ethyl)-4-(4-bromo-1-methyl-1 H-pyrazol-5-yl)-5-methyl-2-thiophenecarboxamide;
N-((1S)-2-amino-1-{[2-(trifluoromethyl)phenyl]methyl}ethyl)-4-{4-chloro-1-methyl-1 H-pyrazol-5-yl)-5-methyl-2-thiophenecarboxamide;
N-((1S)-2-amino-1-{[2-(trifluoromethyl)phenyl]methyl}ethyl)-5-chloro-4-(4-chloro-1-methyl-1H-pyrazol-5-yl)-2-thiophenecarboxamide;
N-((1S)-2-amino-1-{[2-(trifluoromethyl)phenyl]methyl}ethyl)-4-(4-bromo-1-methyl-1 H-pyrazol-5-yl)-5-chloro-2-thiophenecarboxamide;
N-((1*S*)-2-amino-1-{[2-(trifluoromethyl)phenyl]methyl}ethyl)-5-methyl-4-(1-methyl-1 H-pyrazol-5-yl)-2-thiophenecarboxamide;
N-((1*S*)-2-amino-1-{[2-(trifluoromethyl)phenyl]methyl}ethyl)-5-chloro-4-(1-ethyl-1H-pyrazol-5-yl)-2-thiophenecarboxamide;

N-((1*S*)-2-amino-1-{[2-(trifluoromethyl)phenyl]methyl}ethyl)-5-chloro-4-(1,4-dimethyl-1 *H*-pyrazol-5-yl)-2-thiophenecarboxamide;
N-{(1*S*)-2-amino-1-[(3-fluorophenyl)methyl]ethyl}-5-chloro-4-(1-methyl-1H-pyrazol-5-yl)-2-thiophenecarboxamide;
N-{(1*S*)-2-amino-1-[(3-fluorophenyl)methyl]ethyl}-5-chloro-4-(4-chloro-1-methyl-1H-pyrazol-5-yl)-2-thiophenecarboxamide;
N-((1S)-2-amino-1-{[2-(trifluoromethyl)phenyl]methyl}ethyl)-5-ethyl-4-(1-methyl-1H-pyrazol-5-yl)-2-thiophenecarboxamide;
N-((1S)-2-amino-1-{[2-(trifluoromethyl)phenyl]methyl}ethyl)-4-(1,4-dimethyl-1H-pyrazol-5-yl)-5-methyl-2-thiophenecarboxamide;
N-((1S)-2-amino-1-{[2-(trifluoromethyl)phenyl]methyl}ethyl)-4-(4-chloro-1-methyl-1H-pyrazol-5-yl)-5-ethyl-2-thiophenecarboxamide;
N-((1S)-2-amino-1-{[2-(trifluoromethyl)phenyl]methyl}ethyl)-4-(4-bromo-1-methyl-1 H-pyrazol-5-yl)-5-ethyl-2-thiophenecarboxamide;
N-((1S)-2-amino-1-{[2-(trifluoromethyl)phenyl]methyl}ethyl)-4-(1,4-dimethyl-1H-pyrazol-5-yl)-5-ethyl-2-thiophenecarboxamide;
N-((1S)-2-amino-1-{[2-(trifluoromethyl)phenyl]methyl}ethyl)-5-methyl-4-(1-methyl-1 H-pyrazol-5-yl)-2-furancarboxamide;
N-((1S)-2-amino-1-{[2-(trifluoromethyl)phenyl]methyl}ethyl)-4-(4-bromo-1-methyl-1 H-pyrazol-5-yl)-5-methyl-2-furancarboxamide;
N-((1S)-2-amino-1-{[2-(trifluoromethyl)phenyl]methyl}ethyl)-4-(4-chloro-1-methyl-1 H-pyrazol-5-yl)-5-methyl-2-furancarboxamide;
N-((1S)-2-amino-1-{[2-(trifluoromethyl)phenyl]methyl}ethyl)-4-(1,4-dimethyl-1H-pyrazol-5-yl)-5-methyl-2-furancarboxamide;
N-{(1S)-2-amino-1-[(3-fluorophenyl)methyl]ethyl}-4-(4-chloro-1-methyl-1H-pyrazol-5-yl)-5-ethyl-2-thiophenecarboxamide;
N-{(1S)-2-amino-1-[(3-fluorophenyl)methyl]ethyl}-4-(1,4-dimethyl-1H-pyrazol-5-yl)-5-ethyl-2-thiophenecarboxamide;
N-((1S)-2-amino-1-{[3-(trifluoromethyl)phenyl]methyl}ethyl)-4-(1,4-dimethyl-1H-pyrazol-5-yl)-5-ethyl-2-thiophenecarboxamide;
N-((1S)-2-amino-1-{[2-(trifluoromethyl)phenyl]methyl}ethyl)-5-chloro-4-(1-methyl-1 H-pyrazol-5-yl)-2-furancarboxamide;
N-((1S)-2-amino-1-{[2-(trifluoromethyl)phenyl]methyl}ethyl)-5-chloro-4-(4-chloro-1-methyl-1 H-pyrazol-5-yl)-2-furancarboxamide;
N-((1S)-2-amino-1-{[2-(trifluoromethyl)phenyl]methyl}ethyl)-4-(4-chloro-1-methyl-1 H-pyrazol-5-yl)-5-ethyl-2-furancarboxamide;
N-{(1S)-2-amino-1-[(4-fluorophenyl)methyl]ethyl}-4-(4-chloro-1-methyl-1H-pyrazol-5-yl)-5-ethyl-2-furancarboxamide;
N-{(1S)-2-amino-1-[(3-fluorophenyl)methyl]ethyl}-4-(4-chloro-1-methyl-1H-pyrazol-5-yl)-5-ethyl-2-furancarboxamide;
N-{(1S)-2-amino-1-[(3-fluorophenyl)methyl]ethyl}-5-chloro-4-(1-methyl-1H-pyrazol-5-yl)-2-furancarboxamide;
N-{(1S)-2-amino-1-[(4-fluorophenyl)methyl]ethyl}-5-chloro-4-(1-methyl-1H-pyrazol-5-yl)-2-furancarboxamide;
N-((1S)-2-amino-1-{[3-(trifluoromethyl)phenyl]methyl}ethyl)-5-chloro-4-(1-methyl-1 H-pyrazol-5-yl)-2-furancarboxamide;
N-{(1S)-2-amino-1-[(3-fluorophenyl)methyl]ethyl}-5-chloro-4-(4-chloro-1-methyl-1H-pyrazol-5-yl)-2-furancarboxamide;
N-((1S)-2-amino-1-{[3-(trifluoromethyl)phenyl]methyl}ethyl)-5-chloro-4-(4-chloro-1-methyl-1 H-pyrazol-5-yl)-2-furancarboxamide;
N-{(1S)-2-amino-1-[(4-fluorophenyl)methyl]ethyl}-5-chloro-4-(4-chloro-1-methyl-1H-pyrazol-5-yl)-2-furancarboxamide;
N-{(1S)-2-amino-1-[(3-fluorophenyl)methyl]ethyl}-5-chloro-4-{1,4-dimethyl-1H-pyrazol-5-yl)-2-furancarboxamide;
N-{(1S)-2-amino-1-[(4-fluorophenyl)methyl]ethyl}-5-chloro-4-(1,4-dimethyl-1 H-pyrazol-5-yl)-2-furancarboxamide;
N-((1S)-2-amino-1-{[3-(trifluoromethyl)phenyl]methyl}ethyl)-5-chloro-4-(1,4-dimethyl-1H-pyrazol-5-yl)-2-furancarboxamide;
N-((1S)-2-amino-1-{[2-(trifluoromethyl)phenyl]methyl}ethyl)-5-chloro-4-(1,4-dimethyl-1H-pyrazol-5-yl)-2-furancarboxamide;

N-((1S)-2-amino-1-{[3-(trifluoromethyl)phenyl]methyl}ethyl)-5-methyl-4-(1-methyl-1H-pyrazol-5-yl)-2-thiophenecarboxamide;
N-{(1*S*)-2-amino-1-[(4-fluorophenyl)methyl]ethyl}-5-chloro-4-(1-methyl-1*H*-pyrazol-5-yl)-2-thiophenecarboxamide;
N-((1*S*)-2-amino-1-{[3-(trifluoromethyl)phenyl]methyl}ethyl)-5-chloro-4-{1-methyl-1 H-pyrazol-5-yl)-2-thiophenecarboxamide;
N-{(1*S*)-2-amino-1-[(4-fluorophenyl)methyl]ethyl}-5-methyl-4-(1-methyl-1H-pyrazol-5-yl)-2-thiophenecarboxamide;
N-{(1*S*)-2-amino-1-[(3-fluorophenyl)methyl]ethyl}-5-methyl-4-(1-methyl-1H-pyrazol-5-yl)-2-thiophenecarboxamide;
N-((1*S*)-2-amino-1-{[3-(trifluoromethyl)phenyl]methyl}ethyl)-4-(4-chloro-1-methyl-1*H*-pyrazol-5-yl)-5-methyl-2-thiophenecarboxamide;
N-{(1S)-2-amino-1-[(4-fluorophenyl)methyl]ethyl}-4-(4-bromo-1-methyl-1*H*-pyrazol-5-yl)-5-methyl-2-thiophenecarboxamide;
N-{(1S)-2-amino-1-[(4-fluorophenyl)methyl]ethyl}-4-(4-chloro-1-methyl-1*H*-pyrazol-5-yl)-5-methyl-2-thiophenecarboxamide;
N-{(1S)-2-amino-1-[(3-fluorophenyl)methyl]ethyl}-4-(4-chloro-1-methyl-1H-pyrazol-5-yl)-5-methyl-2-thiophenecarboxamide;
N-{(1S)-2-amino-1-[(3-fluorophenyl)methyl]ethyl}-4-(4-bromo-1-methyl-1H-pyrazol-5-yl)-5-methyl-2-thiophenecarboxamide;
N-((1S)-2-amino-1-{[3-(trifluoromethyl)phenyl]methyl}ethyl)-4-(4-bromo-1-methyl-1*H*-pyrazol-5-yl)-5-methyl-2-thiophenecarboxamide;
N-((1*S*)-2-amino-1-{(3-(trifluoromethyl)phenyl]methyl}ethyl)-4-(1,4-dimethyl-1*H*-pyrazol-5-yl)-5-methyl-2-thiophenecarboxamide;
N-{(1S)-2-amino-1-[(3-fluorophenyl)methyl]ethyl}-4-(1,4-dimethyl-1*H*-pyrazol-5-yl)-5-methyl-2-thiophenecarboxamide;
N-{(1*S*)-2-amino-1-[(4-fluorophenyl)methyl]ethyl}-4-(1,4-dimethyl-1H-pyrazol-5-yl)-5-methyl-2-thiophenecarboxamide;
N-{(1*S*)-2-amino-1-[(3-fluorophenyl)methyl]ethyl}-4-(4-bromo-1-methyl-1*H*-pyrazol-5-yl)-5-chloro-2-thiophenecarboxamide;
N-((1*S*)-2-amino-1-{[3-(trifluoromethyl)phenyl]methyl}ethyl)-5-chloro-4-(4-chloro-1-methyl-1 H-pyrazol-5-yl)-2-thiophenecarboxamide;
N-((1*S*)-2-amino-1-{[3-(trifluoromethyl)phenyl]methyl}ethyl)-4-(4-bromo-1-methyl-1*H*-pyrazol-5-yl)-5-chloro-2-thiophenecarboxamide;
N-{(1*S*)-2-amino-1-[(4-fluorophenyl)methyl]ethyl}-4-(4-bromo-1-methyl-1H-pyrazol-5-yl)-5-chloro-2-thiophenecarboxamide;
N-{(1*S*)-2-amino-1-[(4-fluorophenyl)methyl]ethyl}-5-chloro-4-(4-chloro-1-methyl-1H-pyrazol-5-yl)-2-thiophenecarboxamide;
N-{(1*S*)-2-amino-1-[(2,5-difluorophenyl)methyl]ethyl}-4-(4-chloro-1-methyl-1H-pyrazol-5-yl)-5-methyl-2-thiophenecarboxamide;
N-{(1*S*)-2-amino-1-[(2,5-difluorophenyl)methyl]ethyl}-5-methyl-4-(1-methyl-1H-pyrazol-5-yl)-2-thiophenecarboxamide;
N-{(1*S*)-2-amino-1-[(2,5-difluorophenyl)methyl]ethyl}-4-(1,4-dimethyl-1H-pyrazol-5-yl)-5-methyl-2-thiophenecarboxamide;
N-{(1*S*)-2-amino-1-[(2,5-difluorophenyl)methyl]ethyl}-5-chloro-4-(4-chloro-1-methyl-1 H-pyrazol-5-yl)-2-thiophenecarboxamide;
N-{(1*S*)-2-amino-1-[(2,5-difluorophenyl)methyl]ethyl}-5-chloro-4-(1-methyl-1H-pyrazol-5-yl)-2-thiophenecarboxamide;
N-{(1S)-2-amino-1-[(3-fluorophenyl)methyl]ethyl}-4-(4-chloro-1-methyl-1*H*-pyrazol-5-yl)-5-methyl-2-furancarboxamide;
N-((1*S*)-2-amino-1-{[2-(trifluoromethyl)phenyl]methyl}ethyl)-5-(methyloxy)-4-(1-methyl-1 H-pyrazol-5-yl)-2-thiophenecarboxamide;
N-{(11*S*)-2-amino-1-[(4-fluorophenyl)methyl]ethyl}-4-(4-chloro-1-methyl-1*H*-pyrazol-5-yl)-5-methyl-2-furancarboxamide;
N-((1*S*)-2-amino-1-{[3-(trifluoromethyl)phenyl]methyl}ethyl)-4-(4-chloro-1-methyl-1 H-pyrazol-5-yl)-5-methyl-2-furancarboxamide;
N-((1*S*)-2-amino-1-{[2-(trifluoromethyl)phenyl]methyl}ethyl)-4-(4-chloro-1-methyl-1*H*-pyrazol-5-yl-5-(methyloxy)-2-thiophenecarboxamide;

N-{(1*S*)-2-amino-1-[(2,5-difluorophenyl)methyl]ethyl}-5-chloro-4-(1,4-dimethyl-1*H*-pyrazol-5-yl)-2-thiophenecarboxamide;
N-{(1S)-2-amino-1-[(3-fluorophenyl)methyl]ethyl}-4-(4-chloro-1-methyl-1*H*-pyrazol-5-yl)-5-(methyloxy)-2-thiophenecarboxamide;
N-{(1*S*)-2-amino-1-[(4-fluorophenyl)methyl]ethyl}-4-(4-chloro-1-methyl-1*H*-pyrazol-5-yl)-5-(methyloxy)-2-thiophenecarboxamide;
N-((1*S*)-2-amino-1-{[3-(trifluoromethyl)phenyl]methyl}ethyl)-4-(4-chloro-1-methyl-1*H*-pyrazol-5-yl)-5-(methyloxy)-2-thiophenecarboxamide;
N-{(1*S*)-2-amino-1-[(4-fluorophenyl)methyl]ethyl}-4-(1,4-dimethyl-1*H*-pyrazol-5-yl)-5-ethyl-2-thiophenecarboxamide;
N-{(1*S*)-2-amino-1-[(3,4-difluorophenyl)methyl]ethyl}-5-methyl-4-(1-methyl-1*H*-pyrazol-5-yl)-2-thiophenecarboxamide;
N-{(1*S*)-2-amino-1-[(3,4-difluorophenyl)methyl]ethyl}-4-(4-chloro-1-methyl-1*H*-pyrazol-5-yl)-5-methyl-2-thiophenecarboxamide;
N-{(1*S*)-2-amino-1-[(3,4-difluorophenyl)methyl]ethyl}-5-chloro-4-(1-methyl-1*H*-pyrazol-5-yl)-2-thiophenecarboxamide;
N-{(1*S*)-2-amino-1-[(3,4-difluorophenyl)methyl]ethyl}-5-chloro-4-(4-chloro-1-methyl-1 H-pyrazol-5-yl)-2-thiophenecarboxamide;
N-{(1*S*)-2-amino-1-[(3,4-difluorophenyl)methyl]ethyl}-4-(1,4-dimethyl-1*H*-pyrazol-5-yl)-5-methyl-2-thiophenecarboxamide;
N-{(1*S*)-2-amino-1-[(3,4-difluorophenyl)methyl]ethyl}-5-chloro-4-(4-chloro-1-methyl-1 H-pyrazol-5-yl)-2-furancarboxamide;
N-{(1*S*)-2-amino-1-[(3,4-difluorophenyl)methyl]ethyl}-5-chloro-4-(1-methyl-1*H*-pyrazol-5-yl)-2-furancarboxamide;
N-{(1*S*)-2-amino-1-[(3,4-difluorophenyl)methyl]ethyl}-5-methyl-4-(1-methyl-1*H*-pyrazol-5-yl)-2-furancarboxamide;
N-{(1*S*)-2-amino-1-[(3,4-difluorophenyl)methyl]ethyl}-4-(4-chloro-1-methyl-1*H*-pyrazol-5-yl)-5-methyl-2-furancarboxamide;
N-{(1S)-2-amino-1-[(3,4-difluorophenyl)methyl]ethyl}-5-chloro-4-(1,4-dimethyl-1*H*-pyrazol-5-yl)-2-furancarboxamide;
N-{(1*S*)-2-amino-1-[(3,4-difluorophenyl)methyl]ethyl}-4-(1,4-dimethyl-1*H*-pyrazol-5-yl)-5-methyl-2-furancarboxamide;
N-((1*S*)-2-amino-1-{[2-(trifluoromethyl)phenyl]methyl}ethyl)-5-chloro-4-(4-chloro-1-ethyl-1 H-pyrazol-5-yl)-2-thiophenecarboxamide;
N-{(1*S*)-2-amino-1-[(3-fluorophenyl)methyl]ethyl}-5-chloro-4-(4-chloro-1-ethyl-1*H*-pyrazol-5-yl)-2-thiophenecarboxamide;
N-{(1*S*)-2-amino-1-[(4-fluorophenyl)methyl]ethyl}-5-chloro-4-(4-chloro-1-ethyl-1*H*-pyrazol-5-yl)-2-thiophenecarboxamide;
N-((1*S*)-2-amino-1-{[3-(trifluoromethyl)phenyl]methyl}ethyl)-5-chloro-4-(4-chloro-1-ethyl-1 H-pyrazol-5-yl)-2-thiophenecarboxamide;
N-((1*S*)-2-amino-1-{[2-(trifluoromethyl)phenyl]methyl}ethyl)-5-chloro-4-(1-ethyl-4-methyl-1*H*-pyrazol-5-yl}-2-thiophenecarboxamide;
N-{(1*S*)-2-amino-1-[(3-fluorophenyl)methyl]ethyl}-5-chloro-4-(1-ethyl-4-methyl-1*H*-pyrazol-5-yl)-2-thiophenecarboxamide;
N-{(1*S*)-2-amino-1-[(3,4-difluorophenyl)methyl]ethyl}-5-chloro-4-(1-ethyl-4-methyl-1 H-pyrazol-5-yl)-2-thiophenecarboxamide;
N-{(1*S*)-2-amino-1-[(3-fluorophenyl)methyl]ethyl}-5-chloro-4-(1,4-dimethyl-1*H*-pyrazol-5-yl)-2-thiophenecarboxamide;
N-((1*S*)-2-amino-1-{[3-(trifluoromethyl)phenyl]methyl}ethyl)-5-chloro-4-(1,4-dimethyl-1 H-pyrazol-5-yl)-2-thiophenecarboxamide;
N-{(1*S*)-2-amino-1-[(4-fluorophenyl)methyl]ethyl}-5-chloro-4-(1,4-dimethyl-1*H*-pyrazol-5-yl)-2-thiophenecarboxamide;
N-{(1S)-2-amino-1-[(3,4-difluorophenyl)methyl]ethyl}-5-chloro-4-(4-chloro-1-ethyl-1 H-pyrazol-5-yl)-2-thiophenecarboxamide;
N-{(1*S*)-2-amino-1-[(3,4-difluorophenyl)methyl]ethyl}-5-chloro-4-(4-chloro-1-ethyl-1*H*-pyrazol-5-yl)-2-furancarboxamide; and
N-{(1*S*)-2-amino-1-[(3,4-difluorophenyl)methyl]ethyl}-4-(4-chloro-1-ethyl-1*H*-pyrazol-5-yl)-5-methyl-2-furancarboxamide;

or a pharmaceutically acceptable salt thereof.

3. A compound of claim 1 selected from:

N-{(1*S*)-2-amino-1-[(3-fluorophenyl)methyl]ethyl}-5-chloro-4-(4-chloro-1-methyl-1*H*-pyrazol-5-yl)-2-thiophenecarboxamide;
N-{(1*S*)-2-amino-1-[(3-fluorophenyl)methyl]ethyl}-5-chloro-4-(4-chloro-1-methyl-1H-pyrazol-5-yl)-2-furancarboxamide;
N-{(1*S*)-2-amino-1-[(3-fluorophenyl)methyl]ethyl}-4-(4-chloro-1-methyl-1*H*-pyrazol-5-yl)-5-methyl-2-thiophenecarboxamide;
N-{(1*S*)-2-amino-1-[(3,4-difluorophenyl)methyl]ethyl}-5-chloro-4-(4-chloro-1-methyl-1*H*-pyrazol-5-yl)-2-thiophenecarboxamide;
N-{(1*S*)-2-amino-1-[(3,4-difluorophenyl)methyl]ethyl}-5-chloro-4-(4-chloro-1-methyl-1 H-pyrazol-5-yl)-2-furancarboxamide;
or a pharmaceutically acceptable salt thereof.

4. A compound of claim 1 which is:

N-{(1*S*)-2-amino-1-[(3-fluorophenyl)methyl]ethyl}-5-chloro-4-(4-chloro-1-methyl-1 H-pyrazol-5-yl)-2-thiophenecarboxamide;
or a pharmaceutically acceptable salt thereof.

5. A compound of claim 1 which is:

N-{(1*S*)-2-amino-1-[(3,4-difluorophenyl)methyl]ethyl}-5-chloro-4-(4-chloro-1-methyl-1 *H*-pyrazol-5-yl)-2-furancarboxamide;
or a pharmaceutically acceptable salt thereof.

6. A compound according to any one of claims 1 to 5, or a pharmaceutically acceptable salt thereof, for use in therapy.

7. Use of a compound defined in any one of claims 1 to 5 or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating or lessening the severity of a disease or condition selected from cancer and arthritis.

8. The use according to claim 7 wherein said cancer is selected from: brain (gliomas), glioblastomas, Bannayan-Zonana syndrome, Cowden disease, Lhermitte-Duclos disease, breast, inflammatory breast cancer, Wilm's tumor, Ewing's sarcoma, Rhabdomyosarcoma, ependymoma, medulloblastoma, colon, head and neck, kidney, lung, liver, melanoma, ovarian, pancreatic, prostate, sarcoma, osteosarcoma, giant cell tumor of bone, thyroid, Lymphoblastic T cell leukemia, Chronic myelogenous leukemia, Chronic lymphocytic leukemia, Hairy-cell leukemia, acute lymphoblastic leukemia, acute myelogenous leukemia, Chronic neutrophilic leukemia, Acute lymphoblastic T cell leukemia, Plasmacytoma, Immunoblastic large cell leukemia, Mantle cell leukemia, Multiple myeloma Megakaryoblastic leukemia, multiple myeloma, acute megakaryocytic leukemia, promyelocytic leukemia, Erythroleukemia, malignant lymphoma, hodgkins lymphoma, non-hodgkins lymphoma, lymphoblastic T cell lymphoma, Burkitt's lymphoma, follicular lymphoma, neuroblastoma, bladder cancer, urothelial cancer, lung cancer, vulval cancer, cervical cancer, endometrial cancer, renal cancer, mesothelioma, esophageal cancer, salivary gland cancer, hepatocellular cancer, gastric cancer, nasopharangeal cancer, buccal cancer, cancer of the mouth, GIST (gastrointestinal stromal tumor) and testicular cancer.

9. The use according to claim 8 wherein said cancer is selected from: brain (gliomas), glioblastomas, Bannayan-Zonana syndrome, Cowden disease, Lhermitte-Duclos disease, breast, colon, head and neck, kidney, lung, liver, melanoma, ovarian, pancreatic, prostate, sarcoma and thyroid.

10. A pharmaceutical composition comprising a compound according to any one of claims 1 to 5, or a pharmaceutically acceptable salt thereof and a pharmaceutically acceptable carrier.

11. The pharmaceutical composition according to claim 10 which further comprises at least one anti-neoplastic agent.

12. The pharmaceutical composition according to claim 11 wherein the at least one anti-neoplastic agent is selected

from the group consisting essentially of anti-microtubule agents, platinum coordination complexes, alkylating agents, antibiotic agents, topoisomerase II inhibitors, antimetabolites, topoisomerase I inhibitors, hormones and hormonal analogues, signal transduction pathway inhibitors; non-receptor tyrosine kinase angiogenesis inhibitors; immunotherapeutic agents; proapoptotic agents; and cell cycle signaling inhibitors.